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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/488,164	06/07/95	KOPCHICK	J 7707-015

EXAMINER

HM11/1106

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SAOUD, C.
ART UNIT PAPER NUMBER

1646

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DATE MAILED: 11/06/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 10 September 1998

☒ This action is FINAL.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or ~~thirty days~~, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

- ☒ Claim(s) 10-45, 62-63, 65-73 is/are pending in the application.
Of the above, claim(s) 45 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 10-44, 62-63, 65-73 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
- ☐ received.
- ☐ received in Application No. (Series Code/Serial Number) _____
- ☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

- ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- ☐ Notice of Reference Cited, PTO-892
- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
- ☐ Interview Summary, PTO-413
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Notice of Informal Patent Application, PTO-152

-SEE OFFICE ACTION ON THE FOLLOWING PAGES-

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DETAILED ACTION

Response to Amendment

1. Claims 46-61 and 64 have been canceled and claims 65-73 have been added as requested in the amendment of paper #17, filed 10 September 1998. Claims 10-45, 62-63 and 65-73 are pending in the instant application. Claim 45 remains withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.
4. Applicant's arguments filed 10 September 1998 have been fully considered but they are not deemed to be persuasive.

Specification

5. The amendment to the specification at page 12 have not been entered. These amendments are duplicates of amendments which were submitted and entered in paper #11, filed 14 March 1998.

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6. The abstract which was submitted in paper #14 has been entered.

Information Disclosure Statement

Applicant's comments regarding the "Information Disclosure Statement" in paper #14 are noted. The Examiner was not clear in identifying the issue with the references which were provided but not listed on an Information Disclosure Statement. Applicant submitted documents as part of a response to an Office action. MPEP § 609 (C)(3) indicates that these documents may be relied on by Applicant and that

[t]o the extent that a document is submitted as evidence directed to an issue of patentability raised in an Office action, and the evidence is timely presented, applicant need not satisfy the requirements of 37 CFR 1.97 and 1.98 in order to have the examiner consider the information contained in the document relied on by applicant. In other words, compliance with the information disclosure rules is not a threshold requirement to have information considered when submitted by applicant to support an argument being made in a response to an Office action.

At the same time, the document supplied and relied on by applicant as evidence need not be processed as an item of information that was cited in an information disclosure statement. The record should reflect whether the evidence was considered, but listing on a form (e.g., PTO - 892 or PTO - 1449) and appropriate marking of the form by the examiner is not required.

The information which was provided in the previous response of paper #14 was considered as it pertained to the rebuttal of the rejection of the claims. The Office action of paper #15 did not correctly reflect this point.

Applicant has not submitted a PTO-1449 which includes those references which had not been previously cited in the prosecution of the instant application. Applicant states "since they

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were cited and copies provided already, no charge will attach". This is not correct. The submission of the references in the response of paper #14 is sufficient for them to be considered as rebuttal evidence. However, if Applicant wishes them to appear on the face of any patent that may issue from the instant application, they must be submitted as a separate list, preferably on a PTO-1449. Because these references were not properly submitted in paper #14, they are not a proper IDS. Therefore, submission at this time is a submission after a first Office action, but before final and a fee or certification is required (see 37 CFR 1.97(c)). Applicant should note that the references are part of the application but would not appear on the face of any patent that issues from the instant application unless they are submitted as a proper IDS.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 10-44, 62-63 and 65-73 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons of record as applied to claims 10-44 and 46-64.

Applicant argues that reference to the use of the "Micro-Genie" program for secondary structure prediction at page 12 of the specification provides an algorithm for calculating percent identity. This argument is not persuasive because the instant specification never discloses that the "Micro-Genie" program could be used for this purpose or should be used for this purposes over

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any other algorithm which was available to one of ordinary skill in the art. There is no implicit or explicit suggestion in the specification that this program was intended for the calculation of percent identity, therefore, mere reference to this program for the purpose of predicting secondary structure is not support for its use in calculating percent identity. Therefore, as stated in the previous Office action, without a reference to a specific algorithm for calculating percent identity, the metes and bounds of the claims cannot be determined and the claims are indefinite.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 29-33 stand rejected and newly submitted claims 65 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record in paper #12 and 14 as applied to claims 29-33.

Applicant argues that the claims "combine a minimum percentage sequence identity with an activity requirement". However, the recitation of percentage sequence identity (structure) is not sufficient to provide the function (activity) as required by the claim (see page 7 of response). One of skill in the art could not delete nearly half of the growth hormone protein and expect it to bind the receptor in order for it to function as a growth hormone receptor antagonist, absent

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evidence to the contrary. Even if one followed the guidance in the specification relating to regions that are involved in receptor binding, the deletion of non-binding regions would be expected to alter the structure of the protein such that it could no longer bind the receptor, absent evidence to the contrary. Applicant argues that "[t]he only restriction on which AAs are muted how comes from the functional limitation" (see page 7, emphasis omitted). This argument is not persuasive because Applicant is basically claiming any protein that has a particular activity without any guidance as to which modifications could be made to as much as 50% of the protein and still retain the recited activity. The claims are not enabled for their entire breadth because one does not have a reasonable expectation of success that as much as 50% of the protein could be modified and still retain the biological activity recited in the claims. The instant specification provides no examples of any proteins that are so modified that retain the activity and scientific reasoning has been provided as to why the claims are not enabled for the breadth, therefore the claims stand rejected.

Applicant's arguments regarding *In re Hutchison* are noted, but are not persuasive. It is not the practice of the PTO to allow claims based on previously allowed claims by the Office. Each application is reviewed on its own merits and no case law seems to support a conclusion otherwise. Applicant makes reference to Ex parte Mark in support of the current claim language. However, the claims of Mark et al. are not under consideration in the instant application. Applicant argues that "it does not seem to be a great jump from determining which cysteine residues of a given protein are essential to activity to determining which residues of any kind are

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essential, in view of the disclosure of alanine-scanning mutagenesis" (see page 8 of response). This argument is not persuasive for a number of reasons. First, the determination of which cysteines are important in determining biological activity typically require the mutation of but a few amino acids wherein those that are required for activity are usually those that are involved in critical disulfide bond formation. In the instant situation, the claims encompass mutation of up to half of the protein (a very broad claim). Furthermore, alanine-scanning mutagenesis only mutates one amino acid at a time. It is well understood in the art that receptor binding is a coordinated effort of many amino acids throughout the protein. If amino acid position 12 is critical, the mutation of 11 or 13 may alter binding due to amino acid interaction or spacial arrangements that cannot be predicted by alanine-scanning mutagenesis. As stated previously, the claims encompass deletion of 50% of the protein which one of skill in the art would not reasonably expect to bind to the receptor or retain activity. The claims do not include any other structural limitations, therefore, the claims do not have sufficient structure to provide the recited and claimed function, absent evidence to the contrary.

Applicant argues at page 9 of the response that there are several proteins that have identity that is between 66 and 68% and still function (as well as recitation of fish growth hormone identities). However, the issue is not whether there are proteins that differ by as much as 50% and still retain activity, but rather, are the instant claims enabled by the instant specification for their entire breadth? One of ordinary skill in the art would not reasonably expect that deletion of as much as 50% of growth hormone would retain the ability to bind to its receptor. Furthermore,

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modification of as much as 50% of growth hormone by substitution (i.e. with alanine) would not be expected to retain ability to bind to its receptor. The only definite structure that is recited in the claim is that the amino acid corresponding to Gly119 of bovine growth hormone be retained, however, this still is not sufficient to provide the recited activity of the claims.

Applicant argues that there are fragments of growth hormone which retain activity that are only about 20% of the full-length protein. However, the instant claims do not recite those elements that are required for function (namely amino acids 96-133 of bovine growth hormone, see response at page 10). It would appear that these amino acids are required for activity, but not recited in the claims. Therefore, the claims would be incomplete and not enabled for their entire breadth. See *In re Mayhew*, 527 F.2d 1229, 188 USPQ 356 (CCPA 1976).

Conclusion

11. No claim is allowed.

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period

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will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 8AM to 3PM.

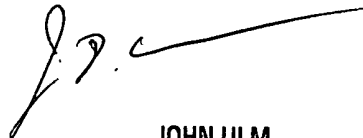
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lila Feisee, can be reached on (703) 308-2731. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Christine Saoud, Ph.D.
November 3, 1998

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JOHN ULM
PRIMARY EXAMINER
GROUP 1800